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09/915,706	07/26/2001	David R. Nelson	5112	9372

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EXAMINER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/915,706	Applicant(s) Nelson
	Examiner Jennifer Graser	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____

2a)☐ This action is **FINAL.** 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above, claim(s) *1, 2, and 29* is/are withdrawn from consideratio

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)

16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9

18)☐ Interview Summary (PTO-413) Paper No(s). _____

19)☐ Notice of Informal Patent Application (PTO-152)

20)☐ Other:

DETAILED ACTION

Election/Restriction

1. I. Claims 1 and 2, drawn to isolated DNA, classified in class 536, subclass 23.1.

II. Claims 3-28, drawn to a mutant strain of *V.anguillarum*, vaccines comprising said strain and immunization methods utilizing said strain, classified in class 424, subclass 234.1.

III. Claim 29, drawn to a hybridization method, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the DNA of Group I may be used for purposes other than hybridization methods, i.e, it may be used to recombinantly produce a protein. Inventions I and II comprise products which are biologically, chemically and structurally different and are, therefore, patentably distinct and independent inventions. The methods of II and III are unrelated as they use different reagents, have different method steps and different objectives. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, as shown by their different

classification, and because the literature search for Groups I-III would not be coextensive, restriction for examination purposes as indicated is proper.

During a telephone conversation with Richard Stevens on February 25, 2003 a provisional election was made without traverse to prosecute the invention of Invention II, claims 3-28. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1, 2 and 29 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Sequence Compliance

2. It is noted that Figures 2-3C of the instant specification recite a nucleotide/amino acid sequence which is encompassed by the definitions for nucleotide sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). The M.P.E.P., Section 2422.02, 37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide/amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide sequences that fall within the definitions. When a sequence is presented in a drawing, regardless of the format or the manner of the presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, **either** in the drawing or in the Brief Description of the Drawings. APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g).

Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Additionally, the instant specification also contains several nucleotide/amino acid sequences throughout the specification which are also encompassed by the definitions for nucleotide/amino acid sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2) and which must conform with the sequence rules for all applications that include nucleotide/amino acid sequences. The sequence identifiers obtained through conformance (paper submission and CRF/electronic) must be inserted into the body of the specification directly following the sequence. Page 8, lines 19-20, and page 10, line 14, were found to contain sequences which are not followed by their appropriate sequence identifier designation. Additionally, Applicants are responsible for meeting compliance with any sequence the Examiner may have inadvertently missed. APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-28 are vague and indefinite because it the mere recitation of a name, i.e., *mugA*, to describe the mutant gene contained in the claimed live, attenuated strain is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. It is unclear what is represented by the name "*mugA*". The specification does not provide a description of this gene's function or it's product's function. It is unclear how one would be able to identify this mutant without knowing the gene's nucleotide sequence or the location of its mutation. The claim should provide any structural properties, such as the nucleotide sequence of the *mugA* gene, which would allow for one to identify the mutant without ambiguity. The mere recitation of a name does not adequately define the claimed strain. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. The claim should be amended to comprise the nucleotide sequence of *mugA*.

Claim Rejections - 35 USC § 112-Scope of Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 3-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "a live, attenuated strain of *V.anguillarum* which comprises a mutation in the *mugA* gene which is set forth in SEQ ID NO:1 wherein said mutation renders the strain incapable of expressing a functional *mugA* protein" and vaccines comprising said strain against *V.anguillarum* in fish and methods for immunizing fish with said strain, does not reasonably provide enablement for "a live attenuated strain of *V.anguillarum* which comprises a mutated *mugA* gene the strain characterized in that it is incapable of expressing a functional *mugA* protein" or for vaccines comprising said strain that protect against *V.anguillarum* in animals or methods for immunizing animals with said strain . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant specification teaches that a live, attenuated mutant designated M93Sm D contains an insertion in the *mugA* gene represented by SEQ ID NO:1 which renders the strain avirulent and able to protect fish against wild-type *Vibrio anguillarum.* The mutant strain disclosed in the instant specification contains an insertion in the *mugA* gene which is represented by SEQ ID NO:1. The specification is silent as to the exact function of the *mugA* gene and it's

gene products. However, it is suggested that the *mugA* gene products may enable the bacterium to better grow in mucus. The claimed mutant was selected on its inability to grow in mucus and its ability to protect against wild-type *Vibrio anguillarum* while not harming the host. The sequence set forth in SEQ ID NO:1 is critical to the invention in that it is needed in order to develop mutants which are avirulent and cannot grow in mucus and which can protect the subject against wild-type *Vibrio anguillarum* . Without the sequence set forth in SEQ ID NO:1, it would take undue experimentation for one of skill in the art to make a mutant with the properties specific to M93SmID and which would have the ability to protect against wild-type *Vibrio anguillarum.* The vaccine art is highly unpredictable and it would take undue experimentation to produce a mutant with the properties of M93SmID by mutating any other gene than SEQ ID NO:1. The method of mutation, i.e., deletion or insertion, is not critical as long as the mutant possesses the desired properties because these techniques were routine in the art at the time the invention was made. However, the gene to be mutated is a critical element and must be claimed. The specification does not identify any other *mugA* gene. As stated above, while the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The present invention is not enabled for mutants with mutations in any other gene except the one set forth in SEQ ID NO:1.

Further, vibriosis is a major bacterial disease affecting fish. All of the studies provided in the instant specific were performed in fish. The phrase "animals" encompasses humans and

other mammals. There is no correlation between the vaccines ability to protect fish from *Vibrio anguillarum* with it's ability to protect humans or mammals. Unless additional evidences are provided in declaratory form which support this broader scope, the claims should be limited to protecting fish and not all 'animals'. The vaccine art is highly unpredictable and challenge experiments are necessary to enable the protection required by the term 'vaccine'. The specification has provided such challenge experiments in fish using a live, attenuated strain of *V.anguillarum* which comprises a mutation in the *mugA* gene which is set forth in SEQ ID NO:1 wherein said mutation renders the strain incapable of expressing a functional *mugA* protein". However, these results do not enable the use of the vaccine in humans or other mammals.

Claim Rejections - 35 USC § 112-Written Description

7. Claims 3-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth the *mugA* gene contained in SEQ ID NO:1 and therefore the written description is not commensurate in scope with the claims drawn to mutants comprising a mutation in *any* mugA gene other than the one set forth in SEQ ID NO:1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a

genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore only "a live, attenuated strain of *V.anguillarum* which comprises a mutation in the *mugA* gene which is set forth in SEQ ID NO:1 wherein said mutation renders the strain incapable of expressing a functional *mugA* protein", but not the full breadth of the claims meets the written description provisions of 35 USC 112, first paragraph.

Status of claims

8. No claims are allowed. The claims are free of the prior art, but must overcome the 112 first and second paragraph rejections and Sequence Compliance problems identified above in order to be allowed.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1641 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JENNIFER E. GRASER
PRIMARY EXAMINER